

AMENDMENTS TO THE CLAIMS

Pursuant to 37 C.F.R. §1.121 the following is a listing of the claims of the present application that will replace all prior versions, and listings, of claims in the application.

Listing of the Claims:

1-11. (Canceled)

12. (Currently amended) An isolated polynucleotide encoding

(a) a T cell receptor (TCR) alpha chain portion containing three alpha complementarity determining regions (CDRs):

CDR1 α : SSYSPS (SEQ ID NO: 2);

CDR2 α : YTSAATL (SEQ ID NO: 3); and

CDR3 α : SPFSGGGADGLT (SEQ ID NO: 5),

or

(b) ~~encoding a modified a variant of the~~ TCR alpha chain portion of (a) wherein up to three amino acid residues in one or more of the said alpha CDRs are replaced by another amino acid residue, and wherein a TCR containing said variant ~~the modified TCR alpha chain portion encoded by the said polynucleotide~~, and a TCR beta chain portion containing three beta CDRs:

CDR1 β : DFQATT (SEQ ID NO: 6);

CDR2 β : SNEGSKA (SEQ ID NO: 7); and

CDR3 β : RDGGEGSETQY (SEQ ID NO: 9),

~~has a greater~~ retains affinity for an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex ~~than a TCR containing the unmodified TCR alpha chain portion.~~

13. (Currently amended) An isolated polynucleotide encoding

(a) a T cell receptor (TCR) beta chain portion containing three beta complementarity determining regions (CDRs):

CDR1 β : DFQATT (SEQ ID NO: 6);

CDR2 β : SNEGSKA (SEQ ID NO: 7); and

CDR3 β : RDGGEGSETQY (SEQ ID NO: 9),

or

~~(b) encoding a modified a variant of the~~ TCR beta chain portion of (a) wherein up to three amino acid residues in one or more of ~~the~~ said beta CDRs are replaced by another amino acid residue, and wherein a TCR containing said variant ~~the modified TCR beta chain portion encoded by the said polynucleotide~~, and a TCR alpha chain portion containing three alpha CDRs:

CDR1 α : SSYSPS (SEQ ID NO: 2);

CDR2 α : YTSAATL (SEQ ID NO: 3); and

CDR3 α : SPFSGGGADGLT (SEQ ID NO: 5),

~~has a greater~~ retains affinity for an HLA-A2/ RMFPNAPYL (SEQ ID NO: 1) complex ~~than a TCR containing the unmodified TCR beta chain portion.~~

14. (Currently amended) An isolated polynucleotide encoding
(a) a single chain TCR molecule containing an alpha chain portion and a beta chain portion,

wherein the alpha chain portion contains three CDRs:

CDR1 α : SSYSPS (SEQ ID NO: 2);

CDR2 α : YTSAATL (SEQ ID NO: 3); and

CDR3 α : SPFSGGGADGLT (SEQ ID NO: 5),

and wherein the beta chain portion contains three CDRs:

CDR1 β : DFQATT (SEQ ID NO: 6);

CDR2 β : SNEGSKA (SEQ ID NO: 7); and

CDR3 β : RDGGEGSETQY (SEQ ID NO: 9),

or

(b) a variant of the encoding a modified single chain TCR molecule of (a) wherein up to three amino acid residues in one or more of said the CDRs are replaced by another amino acid residue, wherein the variant modified TCR encoded by the said polynucleotide has a greater retains affinity for an HLA-A2/ RMFPNAPYL (SEQ ID NO: 1) complex ~~than a TCR containing the unmodified CDRs.~~

15. (Currently amended) An expression vector comprising [[a]] the polynucleotide according to any one of claims 12 to 14.

16. (Currently amended) [[An]] The expression vector according to claim 15 which is a retroviral vector.

17. (Currently amended) A host cell comprising [[a]] the polynucleotide according to any one of claims 12 to 14.

18. (Currently amended) [[A]] The host cell according to claim 17 which is a T cell.

19. (Currently amended) [[A]] The host cell according to claim 18 which is a T cell derived from a patient.

20. (Withdrawn, Currently amended) A method of combating a WT1-expressing malignancy in a patient, the method comprising introducing into the patient a T cell, preferably derived from the patient, which is modified to express the polynucleotide of any one of claims 12 to 14.

21. (Withdrawn, Currently amended) A method according to claim 20 comprising (1) obtaining T cells from the patient, (2) introducing into the T cells [[a]] the polynucleotide according to any one of claims 12 to 14 so that the T cell expresses the encoded TCR molecule and (3) introducing the cells from step (2) into the patient.

22. (Withdrawn, Previously presented) A method according to claim 20 wherein the WT1-expressing malignancy is any one or more of breast cancer, colon cancer, lung cancer, leukaemia, ovarian cancer, melanoma, head and neck cancer, thyroid cancer, glioblastoma and sarcoma.

23-24. (Canceled)

25. (Withdrawn, Currently amended) A method of selecting a TCR molecule with improved binding to an HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex comprising (a) expressing the polynucleotide of any one of claims 12-14, (b) determining whether the TCR molecule expressed by the polynucleotide of any one of claims 12-14 binds to an HLA-A2/ RMFPNAPYL (SEQ ID NO: 1) complex with greater affinity than a TCR molecule without the replacement amino acid(s), and (c) selecting a polynucleotide encoding a TCR molecule which binds with greater affinity to the HLA-A2/RMFPNAPYL (SEQ ID NO: 1) complex.

26-27. (Canceled)

28. (Currently amended) A host cell comprising [[an]] the expression vector according to claim 15.

29. (Currently amended) [[A]] The host cell according to claim 28 which is a T cell.

30. (Currently amended) ~~[[A]]~~ The host cell according to claim 28 which is a T cell derived from a patient.

31. (Previously presented) A method of combating a WT1-expressing malignancy in a patient, the method comprising introducing into the patient a T cell modified by the expression vector of claim 15.

32. (Previously presented) A method according to claim 31 wherein the WT1-expressing malignancy is any one or more of breast cancer, colon cancer, lung cancer, leukaemia, ovarian cancer, melanoma, head and neck cancer, thyroid cancer, glioblastoma and sarcoma.

33. (New) The polynucleotide of claim 12 wherein the alpha CDRs of said variant differ from the alpha CDRs of the TCR alpha chain portion of (a) by up to three amino acid replacements.

34. (New) The polynucleotide of claim 12 wherein said up to three amino acid residues are replaced with conservative replacement amino acids.

35. (New) The polynucleotide of claim 13 wherein the beta CDRs of said variant differ from the beta CDRs of the TCR beta chain portion of (a) by up to three amino acid replacements.

36. (New) The polynucleotide of claim 13 wherein said up to three amino acid residues are replaced with conservative replacement amino acids.

37. (New) The polynucleotide of claim 14 wherein the CDRs of said variant differ from the CDRs of the single chain TCR molecule of (a) by up to three amino acid replacements.

38. (New) The polynucleotide of claim 14 wherein said up to three amino acid residues are replaced with conservative replacement amino acids.